UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,337	07/14/2006	Akira Nishiyama	Q95734	2433

23373 7590 01/07/2009

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
01/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,337	NISHIYAMA ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 10-13* is/are pending in the application.

4a) Of the above claim(s) *4-6,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,10 and 13* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendment of 10/30/08 is entered.

Claims 1 is amended.

Claims 7-9 are cancelled.

Claims 1, 3-6, and 10-13 are presently pending.

Election/Restrictions

Applicant's election without traverse of Invention I, Claims 1-10, and the species of Candida, encompassed in Claims 1-3 and 7-10 in the reply filed on 11/16/07 is acknowledged.

Claims 4-6 and 11-12 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/16/07.

Claims 1-3, 10, and 13 are presently considered.

Notice: Claim Identifiers

Claim 13 is missing the bracket after the claim identifier "previously presented". Please make sure the claims are perfect, as it only obfuscates prosecution to be sloppy with the claims. However, as it appears Applicant is acting in good faith, the claims have been nonetheless entered. Future errors may lead to a notice of non-responsive amendment.

Information Disclosure Statement

Further review on the part of the Examiner has determined that the office's policy is for me to sign off on documents due to the opinion given by others in examining other Applications, which may not even be US applications, or even in English. Hence, the Examiner has now signed off on the Letunova document.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The advisory of record that should claim 10 be found allowable, claim 13 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, is withdrawn.

To wit, Applicant has amended claim 1 to remove Claim 10 from having the same scope as Claim 13.

Claim Objections

Claim 3 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form. Claim 3 is drawn to a broader genus of products of organisms than are encompassed in the parent claim, Claim 1. To wit, Claim 3 contains Rhodococcus and Rhodotorula, which are not contained in Claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, and 10 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites that the enzyme source is any product that has the activity of selectively reducing the compound, which "belongs to genus *Candida* or genus *Devosia* and/or an enzyme obtained from any of these microorganisms ***and*** … is a cultured product of [several HB101 cells containing specific plasmids] and/or any enzyme obtained from these microoganisms". The metes and bounds of such are unclear. If it must be a genus Candida or Devosia, how can it also be limited to HB101s containing specific plasmids? It appears to the Examiner that Applicant is claiming anything from these various cell types rather than the specifically described proteins which produce the activity, and really just reaching through. For simplicity, the Examiner has chosen to read the claim to encompass any enzyme or source of enzyme, even it does not contain the enzyme which has the activity. Claim 3 is worse, adding in new organism generae, but such further emphasizes Applicant's intent to reach through by effect, and failure to do so by

introducing the lack of clarity as to what is being claimed. Hence, Claims 1, 3, and 10 are unclear for their metes and bounds.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of the amendments, the rejections of Claim 1 under 35 U.S.C. 102(b) as being anticipated by Whitney, et al. (1972) Advances in Chemistry, Vol. 130: 270-80, is withdrawn.

To wit, due to the amendments, and not due to the argument, the specific enzymes are not found in Whitney.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

While the rejections of Claims 1 and 10 are withdrawn due to the amendments (i.e., absence of the specific enzymes listed in claim 1 from the Whitney citation):

Claim 13 remains rejected, under 35 U.S.C. 103(a) as being unpatentable over Whitney, et al. (1974) Advances in Chemistry, Vol. 130: 270-80 and the general knowledge in the art, for reasons of record.

Whitney teaches the reduction of 5-hydroxy-2-pentanone by chelated lithium compounds, to yield optically active 1,4-pentanediol (e.g., p. 277). Moreover, the compounds exhibit stereoselective reduction, otherwise the resultant compound would not be optically active.

However, Whitney does not teach obtaining the compound for reduction from a method comprising acid hydrolysis of 2-hydroxy-gamma-butyrolactone.

On the other hand, it is well known that 2-hydroxy-gamma-butyrolactone has been available for years, and even Applicant's specification states that the availability of such is superior to other sources, evidencing Applicant's acknowledgement of the Art. This is Official Notice.

Second, it is instantly recognizable to the Artisan, who is aware of organic chemistry, that an acid hydrolysis, followed by a reduction by LiAlH4 will yield the alcohol of formula 2.

Hence, at the time of the invention, the claimed invention would have been obvious. The Artisan would be motivated to perform the acid hydrolysis to perform a reduction and thereby obtain the compound of interest. Moreover, the Artisan would have had a reasonable expectation of success, as the art of organic chemistry was already fleshed out for the methods involved in such syntheses.

Response to Argument – 103 - Whitney and general knowledge

Applicant's argument of 4/25/08 has been fully considered but is not found persuasive.

Applicant argues that Whitney does not disclose the use of 2-acetyl-gamma-butyrolactone as the source of 5-hydroxy-2-pentanone and subsequent reduction to optically active 1,4-pentanediol (p. 12, paragraphs 2-3).

Such is true, but not persuasive. The Examiner never said that Whitney discloses the use of 2-acetyl-gamma-butyrolactone to make 5-hydroxy-2-pentanone.

Applicant argues that even if the Artisan would recognize that such a reaction would take place, it does not mean that the Artisan would employ 2-acetyl-gamma-butyrolactone as the source of 5-hydroxy-2-pentanone (p. 12, last paragraph - p. 13, paragraph 4).

Such is not persuasive. Certainly, availability, as shown in the rejection, is one reason of non-specific motivation to utilize such compound as the source. Moreover, basic organic chemistry dictates the reaction, and hence, the Artisan does know that the reaction would take place. For Example, Run 13 of Whitney (TABLE 1) demonstrates the reaction that 5-hydroxy-2-pentanone would produce 1,4-pentanediol. In addition, it is clear that acid hydrolysis of 2-acetyl-gamma-butyrolactone produces 5-hydroxy-2-pentanone (e.g., the opening of the butyrolactone by acid hydrolysis (p. 680) and decarboxylation of the keto-acid (p. 853) as shown in Morrison and Boyd (1974) Organic Chemistry, 3rd Edition, Published by Allyn and Bacon, New York, NY., pages as quoted).

Applicant argues that they have shown that the storage of 2-acetyl-gamma-butyrolactone provides problems of storage of 2-keto pentanol, And hence, it is patentable over the Art (p. 13, penultimate paragraph).

Such is not persuasive. Applicant has not claimed a storage method, but an obvious chemical reaction. It is standard in patent claims to be commensurate with your invention.

Applicant argues that they can rely upon unexpected results to obtain patentability over otherwise obvious art, even as evinced in KSR v. Teleflex, and hence, they are due patentability (pp. 13-14).

Such is not persuasive. While Applicant is correct, and unexpected results may be patentable, the unexpected result must be part of the claim to be patentable. Here, the claim is to an obvious chemical reaction, and there is nothing unexpected about utilizing distinct steps and starting materials predicted in the art to yield the same product.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-10 and 13 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes encoded in pNTS1G, pNTFPG, pNTDRG1, pNTRS, and pNTRGG1, to produce R, R, R, S, and S enantiomers, respectively, does not reasonably provide enablement for the breadth of products (e.g., enzyme sources, enzymes) and the breadth of organisms and the breadth of enantiomers for any particular source, for reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is noted that Applicant has attempted to amend Claim 1 to indicate that the scope is limited to the plasmids in the claim, however, as is indicated under the 112/2nd rejections, the

claims are not clear as to their true scope, the claiming of "enzyme source" rather than a fraction containing the enzyme encoded byt he protein, and further dependent claims which claim other bacteria than the organisms of claim 1, indicate that Applicant is intending, in one reasonable interpretation, broader than simply the proteins encoded by these plasmids.

The substance of the rejection is restated for convenience, but is not modified from the last rejection.

The encompass the production of optically active 1,4-pentanediol from 5-hydroxy-2-pentanone, by any enzyme source having the activity of steroselectively reducing the pentanone. The enzyme source can be any cultured product of various microorganisms (Claim 3), indicating that the enzyme source may be derived of any organism in the broad claims. The enzyme source can be of any genus Candida or Devosia, Candida malis, or Candida magnoliae, or any enzyme obtained from these to obtain the R-isomer (Claims 7-8), indicating that the broad claims encompass the use of these same enzyme sources to produce the S isomer. FERM BP-8535, 7117, or 08458, or any enzyme obtained from such may be used to produce the R isomer (Claim 9), indicating that the broad claims go beyond these specific deposits, as well as include a broad range of enzymes. Claims 10 and 11 are limited to the use of a specific precursor to obtain the pentanone, however, are also subject to the breadth of enzymes and sources and isomers.

The nature of the invention is the selective reduction of 5-hydroxy-2-pentanone with any enzyme to produce optically active 1,4-pentane diol. The invention is generally enabled for the use of standard organic chemistry methods, e.g., Whitney, et al. (1974) Advances in Chemistry, Vol. 130: 270-80. The organic chemist is well aware of organic chemistry, and the methods to produce the product are generally within the grasp of the organic chemist without undue

experimentation. However, the claims also, importantly, encompass the use of biochemical enzymes (i.e., protein enzymes) to produce the same. This is where the problems in the Art exist.

The closest Prior Art with regard to biochemical reductions are those of Wada, et al. (1999) Journal of Bioscience and Bioengineering, 87(2): 144-48 and Wada, et al. (1998) Bioscience and Biotechnological Biochemistry.

The Wada (1998) article teaches and reviews a general characterization of several enzymes from various organisms, which produce stereoselective reductions of a distinct molecule, which have stereoselectivity which is not commensurate with any specific enantiomer, such that, from this Article, the Artisan could not reasonably predict that any particular enantiomer would be made in any specific organism (DISCUSSION), other than that the specific enzyme will produce the product found.

The Wada (1999) article teaches several enzymes derived from a specific species of Candida which have distinct activities with regard to the reduction of specific chemicals (e.g., TABLE 2).

However, commensurate with Applicant's argument of 4/25/08 (pp. 12-13), it is clear that Wada also notes that several substrates will not work with specific enzymes, and there is simply no way to reasonably predict which of the enzymes, or which other enzymes will produce the activity required of reducing the pentanones and with the stereoselectivity required, in any specific embodiment.

Applicant's specification Broadly teaches many sources of enzyme and broadly states that these enzymes may be used to obtain the various isomers with the various stereoselectivity.

Applicant's examples teach specific encoded deposits of enzymes pNTS1G, pNTFPG, pNTDRG1, pNTRS, and pNTRGG1, without reference to which enzyme is which, and from where it is obtained. Hence, the Examiner cannot determine more from this than that the specific enzymes will work.

Still further, it is clear from the specification, that the enzyme source is self-determining (e.g., definiton of Enzyme Source, p. 14), without any more elaboration as to which enzyme sources actually have the activity.

Therefore, the Artisan would have to experiment to find those sources that would produce the required reduction, and determine which isomer would be produced (i.e., S or R), as well as determine those enzymes encompassed which produce the particular activity.

Such experimentation is considered undue as it is required to reasonably predict the breadth of Applicant's claimed invention for Applicant.

Response to Argument – Enablement

Applicant's argument of 10/30/08 has been fully considered but is not found persuasive.

Applicant argues that Claim 1 has been amended to the enzyme source of previous Claim 9, and hence is clearly enabled (p. 16, paragraph 1).

Such is not persuasive. First, Claim 1, as amended, states that the R-isoform may be from a genus *Candida, Devosia,* and is also specifically any enzyme from these organisms, rather than the specific enzymes which are enabled, and is also HB101s transformed with plasmids encoding various proteins, and it is also any enzyme from these organisms, rather than the enzyme of the plasmid. How these enzymes and enzyme sources are the enzymes which are enabled, while it is clear that the source or any other enzyme from the source makes no sense to

the Examiner. Still further, Claim 3 brings in two more genera: Rhodococcus and Rhodotorula, or any enzyme from these organisms. This means that Applicant is attempting to claim even more material which is clearly not enabled. Hence, Applicant's argument is clearly not in line with their claimed invention, as presently claimed.

Applicant argues that Claim 13 does not require the enzyme sources, and hence, is not required to be enabled for such (p. 16, paragraph 2).

Such is not persuasive. Applicant's specification teaches that biological enzymes are encompassed by the methods claimed, and hence, the claim clearly needs to be enabled for such. Simply because Applicant only discusses biological enzymes as enzymes of the invention does not mean that other enzymes do not exist, but it also does not mean that they do not intend to claim biological enzymes in Claim 13, especially when Claims 1 and 10 clearly encompass biological enzymes.

Conclusion

No Claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Examiner of Art Unit 1633